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The Broad Street Pump

SEIB Colloquium 2011

Professor Tania Sorrell and A/ Professor Ben Marais
Sydney Emerging Infections and Biosecurity Insitute
University of Sydney

SEIB 2011, our annual colloquium, hosted on the 23rd and 24th of November, at the New Law School Building on Camperdown campus, was opened by the Dean of the Sydney Medical School, Professor Bruce Robinson. The forum provided a platform to update colleagues on achievements within SEIB, allowing them to share research findings and interests, facilitate cross-disciplinary exposure and exchange of ideas, and focus on specific thematic areas that represent areas of strength that could be developed into future funding applications. Brief post-graduate student presentations and posters added impetus to discussion of the multidisciplinary nature of our work. Selected representative abstracts from these presentations are included in this issue of BSP.

Three main themes were explored: 1) Microbial ecology and antimicrobial resistance 2) Social networks, outbreaks & communications and 3) Food security and safety.

Leading speakers from different faculties presented their research results and personal experience, followed by interactive panel discussions to identify critical outstanding questions, areas of mutual interest and possibilities for future project proposals. (*Continued on next page…)*

Inside this issue

Events

(*Cont'd*)
An outstanding keynote lecture on "Malaria – targeting parasite and host kinomes", with an emphasis on kinases as potential drug targets, was delivered by Professor Christian Doerig, newly appointed head of the Department of Microbiology at Monash University, Melbourne.

The annual Beveridge lecture at the School of Veterinary Science was given by Dr David Jordan from the NSW Department of Primary Industries, on the topic of antimicrobial use in prophylaxis, pre-emptive and targeted therapy in livestock and companion animals, with an emphasis on methicillin resistant *Staphyloccus aureus* (MRSA) infections. In a stimulating address, he highlighted the need to move beyond the current narrow regulatory focus on residue levels within animal products, which is an incomplete marker of potential harm, to a broader appreciation of antibiotic-associated disturbances of microbial ecology, selection of potential pathogens and transmission between animals and humans.

Colleagues from the Social Sciences also delivered key presentations. Dr. Alana Mann from the Department of Media and Communications and A/Professor Ian Kerridge from the Centre for Values, Ethics and the Law (VELIM) led a viewpoint discussion on how the media, especially the print media, frame emerging infectious diseases. Dr. Olaf Werder explored the social ecological model as a framework when communicating about infectious diseases.

SEIB has been active during 2011 in the Asia-Pacific region. Initiatives include an NHMRC-funded tuberculosis field trial, Public Health laboratory capacity building and training in clinical skills in Vietnam; nascent collaborations with the Pasteur institute in Cambodia, capacity building in health in Timor L'Este and research collaborations in social, veterinary and health sciences in Indonesia.

We wish to thank Ms Emma Butschek, our Executive Support officer, and all other contributors for their outstanding efforts in making SEIB 2011 a great success.

Professor Tania Sorrell and A/ Prof Ben Marais

WINNER—MRSA Grant

An outbreak of Methicillin-Resistant Staphylococcus Aureus (MRSA) rapidly identified in a Neonatal Intensive Care Unit (NICU) using routine subtyping-based surveillance

Matthew V. N. O'Sullivan, Angie Pinto, Fei Zhou, Vitali Sintchenko, Gwendolyn L. Gilbert

Centre for Infectious Diseases and Microbiology
Institute of Clinical Pathology and Medical Research, Westmead Hospital

Identifying nosocomial MRSA acquisition in high prevalence settings is often only possible using molecular subtyping, but routine subtyping is not practical using existing methods. We have developed a rapid, high-throughput, inexpensive, highly discriminatory typing system for molecular characterisation of MRSA which we have introduced routinely to quickly identify outbreaks of MRSA in our institution.

The typing method interrogates 19 binary targets using a multiplex PCR based reverse-line blot assay. All MRSA isolates from hospital inpatients are typed and the assay is performed at least weekly. When indistinguishable isolates are identified, temporospatial case information is collected to determine if nosocomial transmission may have occurred, and if so, an infection control investigation is launched.

Since April 2011, 13 infants with MRSA infection or colonisation were identified in the NICU of our institution, two of whom died. 10 of these had a binary typing pattern which was indistinguishable. This outbreak strain was also detected on further screening in one staff member and from an environmental sample. The remaining 3 infants, 3 other staff members, and 3 mothers were colonised with different MRSA strains.

Routine molecular subtyping-based infection control surveillance can quickly and clearly identify outbreaks of nosocomial infection, and aid in undertaking targeted infection control interventions.

WINNER—Best Oral Presentation

Influenza, Wind, Humidity and Air Temperature – a survival analysis of Equine Influenza spread

Simon Firestone[1], Naomi Cogger[2] Barbara Moloney[3], Jenny-Ann Toribio[1], Michael Ward[1], Navneet Dhand[1]

[1]Faculty of Veterinary Science, The University of Sydney, 425 Werombi Road, Camden, NSW, Australia
[2]The EpiCentre, Institute of Veterinary Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand
[3]New South Wales Government Department of Primary Industries, Principal Department of Trade & Investment, Regional Infrastructure & Services, Orange, NSW, Australia

The influence of humidity and temperature on the transmission of influenza A viruses have recently been established under controlled laboratory conditions. The interplay of meteorological factors during actual influenza epidemics is less clear. We applied survival analysis on data from the 2007 epidemic of equine influenza (A/H3N8) in Australia together with concurrent daily meteorological data, to quantify the hazard of infection associated with air temperature, humidity and wind velocity.

Meteorological conditions at each premises location were estimated by smoothing daily meteorological data, and analysed as time-varying covariates using Cox regression. Meteorological covariates time-lagged by 3 days were strongly associated with influenza infection, corresponding with the incubation period of equine influenza. An interaction was detected between relative humidity and air temperature ($p<0.01$), validating a previously reported relationship, under field conditions. Strong winds (> 30 km hour^{-1}) from the direction of the nearest infectious premises were also strongly associated with infection ($p=0.02$).

Our empirical analysis supports, and extends, the findings of recent studies into influenza transmission conducted under laboratory conditions. The relationships described are of direct importance for managing influenza epidemics in horses, and more generally, may inform the modeling of epidemics of other infectious diseases of both humans and animals.

Acknowledgements
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WINNER—Best Poster

An inhaled triple antibiotic dry powder formulation for the treatment of Tuberculosis

John Chan, Kim Chan, Paul M Young, Daniela Traini

Faculty of Pharmacy, Advanced Drug Delivery Group, The University of Sydney

Treatment of tuberculosis (TB) with the standard oral antibiotic regimen is effective but inefficient, requiring high drug dosing and lengthy treatment times. Three concurrent first-line antibiotics are recommended by the World Health Organisation (WHO) guidelines: pyrazinamide, rifampicin and isoniazid, given daily in a ratio of 400:150:75mg, respectively . A novel formulation for dry powder inhalation (DPI) combining these antibiotics, may facilitate rapid and efficient resolution of local and systemic infection.

A solution of the antibiotics at the WHO-recommended ratio was spray dried. The collected powder was assessed by scanning electron microscopy, x-ray diffractometry and laser diffraction. Twenty milligrams of the DPI formulation was weighed into a size 3 HPMC capsule and loaded into an Aerolizer™ DPI device for dispersion via an *in vitro* aerosol sizing apparatus (multi-stage liquid impinger) then analysed by HPLC.

Particles obtained were spherical, distinct and crystalline. A mass median aerodynamic diameter of 2.3 ± 0.1µm, and fine particle fraction (<5µm) of 45 ± 2.5%, indicate superior aerosol performance. Quantitative analysis indicates individual particles contained the three antibiotics at the expected proportions (400:150:75 w/w).

This excipient-free triple antibiotic DPI formulation could be a significant treatment for TB with efficacy to be assessed in upcoming *in vivo* studies.

An exotic mosquito exploits cryptic urban habitats in southern Australia: implications for water conservation strategies and mosquito-borne disease risk

Kassim, N.F.A, Webb, C.E. and Russell R.C

The Department of Medical Entomology, The University of Sydney and Institute of Clinical Pathology and Medical Research Westmead Hospital

In response to potential water shortages resulting from climate change, Australian cities are developing strategies to conserve and recycle water. Water sensitive urban design elements, that include above- and below-ground water storage, are increasingly incorporated into residential, recreational and industrial developments.

The mosquito Culex Molestus is thought to have been introduced into Australia in the 1940s and concern has been raised as to the potential role this species may play in the transmission of endemic and exotic arboviruses.

A series of controlled laboratory experiments were conducted to investigate the biology and ecology of this species and found that it was strongly stenogamous (i.e. the mosquito successfully mates in confined spaces) and over 95% of females laid autogenous egg rafts (i.e. a blood meal was not required for the first batch of eggs). Immature mosquitoes raised under low temperatures and poor larval nutrition still maintained the ability to produce autogenous egg rafts.

The results of this investigation indicate that, unlike the majority of Australian mosquitoes that are dependent on a vertebrate blood meal and above ground habitats for egg-laying and larval development, Cx. molestus has perfectly adapted to subterranean habitats and this adaptation allows the mosquito to remain active throughout the year in close association with human habitation.

Dr. Rosie Sadsad PhD, MEng, BEng

Name: Dr. Rosie Sadsad PhD, MEng, BEng
Position: CIDM-PH Postdoctoral Fellow in Infectious Diseases Informatics
Phone: (+612) 9845 5973
Email: rosemarie.sadsad@swahs.health.nsw.gov.au

Rosie Sadsad is a Postdoctoral Research Fellow at the Centre for Infectious Diseases and Microbiology - Public Health. She conducted her PhD research at the Centre for Health Informatics, University of New South Wales and is qualified as a Computer and Biomedical Engineer (B. Computer Eng, M. Biomed Eng, 2004). Her research interests include the application of modeling and simulation to public health. She is currently involved with developing a system to alert infection control of potential MRSA transmission events and/or MRSA outbreaks in the hospital. As part of her PhD, she developed a simulation model to evaluate several hospital infection control policies for reducing the prevalence and incidence rate of MRSA infections. She has worked as a research assistant for the Dementia Collaborative Research Centre where she developed models that project the prevalence of dementia and evaluates treatment therapies for behavioral and psychological symptoms of dementia (BPSD). She has also worked as a research assistant at the Victor Chang Cardiac Research Institute applying bioinformatics to heart disease research.

PPARα agonist WY14643 improves the antiviral effect of interferon against Hepatitis C virus

Read S.A, George J., Douglas M.W

Storr Liver Unit, Westmead Millennium Institute, Westmead Hospital and The University of Sydney

No vaccine is currently available for Hepatitis C virus (HCV) infection. If untreated, chronic infection develops in up to 80% of individuals, increasing their likelihood of developing steatosis, cirrhosis and hepatocellular carcinoma (HCC).While treatment with interferon, ribavirin and more recently viral protease inhibitors can cure chronic infection, a significant proportion of individuals, especially those infected with HCV genotypes 1 and 4,do not respond to therapy.Interestingly, the HCV genotypes that are resistant to treatment are also those more likely to induce insulin resistance, which can be reversed after eliminating the virus. We therefore examined the effect of insulin sensitisers on response to interferon treatment in vitro.

Using the human hepatoma cell line Huh-7 infected with the JFH-1 strain of HCV, we examined the effects of metformin (AMPK activator), pioglitazone (PPARγ agonist) and WY14643 (PPARα agonist) on the interferon response. We found that WY14643 best enhanced the effects of interferon on inhibiting virus replication. Chronic exposure to interferon reduces the sensitivity of interferon stimulated genes (ISGs) to subsequent interferon treatment, and occurs in many patients with chronic hepatitis C. In our model WY14643 partially restored the sensitivity to interferon, and dramatically reduced the expression of several negative regulators of the interferon signalling pathway. Our data suggests that PPARα agonists may improve clinical response to IFN treatment in patients with HCV infection.

Detection of *Strongyloides Stercoralis* in stool using the Loop Mediated Isothermal Amplification (Lamp) Method

MR Watts, R Lee, GS James, Y Sultana, AC Outhred, FR Kong, JR Iredell, SCA Chen

Department of Microbiology, Centre for Infectious Diseases and Microbiology Institute of Clinical Pathology and Medical Research, Westmead Hospital

Strongyloides stercoralis is an important parasitic nematode that may cause chronic infections. These range in severity from asymptomatic to fatal. The most effective conventional methods for detection in stool require live larvae. Nucleic acid detection would allow easier specimen transport in ethanol. This also avoids the risk of laboratory-acquired infection.

Aim: To apply loop-mediated isothermal amplification (LAMP) of nucleic acid for the detection of *S. stercoralis* DNA in stool.

Methods: Primers specific to the strongyloides 28S rRNA gene were designed. The LAMP reaction was optimised using *Strongyloides ratti* from culture. LAMP products were characterised with restriction enzyme digestion and cloning with sequence analysis. Analytical sensitivity was determined using serial dilutions of a PCR product and stool specimens spiked with *S. ratti*. Specificity was tested using 30 normal stool controls and DNA from a range of bacteria, fungi and parasites. Clinical specimens containing *S. stercoralis* were tested.

Results: The assay showed good analytical sensitivity and specificity. *S. stercoralis* and spiked *S. ratti* were detected in human stool specimens.

Discussion: LAMP assays can be performed using simple equipment and are suited to settings that are resource-limited. These results indicate that LAMP may be effective for the detection of *S. stercoralis* in stool.

Upcoming Events...

Infection Control Workshop—May 3 and 4 2012

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Centre for Infectious Diseases and Microbiology - Public Health

Mailing Address: PO Box 533, Wentworthville NSW 2145

Phone: (612) 9845 6255

Email: seib@sydney.edu.au or lyn.gilbert@sydney.edu.au

- **SEIB**

Sydney Emerging Infections and Biosecurity Institute

Mailing Address: ICPMR Bldg Rm 3114, Westmead Hospital, Westmead, NSW 2145

Phone: (612) 9845 9864

Email: seib@sydney.edu.au